Original Article

Associations between With-The-Rule and Against-The-Rule Astigmatism and Higher-Order Aberrations in Compound Myopic Astigmatism

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ABSTRACT

Purpose: To examine the relationship between astigmatism axis and higher-order aberrations (HOAs) in patients with compound myopic astigmatism**.**

Study Design: Cross-sectional descriptive study.

Place and Duration of Study: Cornea Clinic in the Shiraz University of Medical Science, Shiraz, Iran, from 2018-2020.

Methods: A total of 1370 right eyes, aged 18-40 years, were included in the study. Subjective cycloplegic refraction and distance aberrometry, measured with a Shack-Hartmann device, were analyzed. Zernike components of horizontal coma (Z_3^1), vertical coma (Z_3^{-1}), oblique trefoil (Z_3^3), vertical trefoil (Z_3^{-3}), spherical aberration, and total root-mean-square wave-front errors for 6 mm pupils were analyzed. With the rule and against the rule astigmatism groups were defined based on vector analysis for the astigmatism axis (J0 and J45). Positive and negative values of J0 indicate with-the-rule and against-the-rule astigmatism, respectively. Spearman's correlations were calculated between HOAs and J0.(To simplify evaluation, we did not consider J45 in analysis which indicates oblique astigmatism).

Results: The mean age was 29.01±5.19. The mean spherical equivalent (SEQ) was -3.64 ± 1.59D, range [-0.75 to -10.00 D] and the mean cylindrical power was -1.01 ± 0.95D, range [0 to -5.00D]. J0 correlates positively with vertical coma (Z_3^{-1}) ($r = 0.1$ $p < 0.001$) and negatively with oblique trefoil(Z_3^3), ($r = -0.1$, $p < 0.001$).

Conclusion: We found weak systematic correlations between third-order aberrations and the astigmatism axis. Increasing against-the-rule is associated with a positive shift in oblique trefoil (Z_3^3) and a negative shift in vertical coma (Z_3^{-1}).

Keywords: Higher-order aberration, myopia, astigmatism, coma, spherical aberration.

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INTRODUCTION

Higher order aberrations(HOAs) may provide optical signals that contribute to the development of sphero-cylindrical refractive error.[1-4] It was suggested that increasing negative spherical aberration (Z_4°) with accommodation might significantly reduce the retinal image quality and promote near-work-induced myopia.[4,5] In the context of blur-driven refractive error, a previous computational modeling study has hypothesized that negative-vertical coma (Z_3^{-1}) and positive-oblique trefoil (Z_3^3) may signal with-the-rule (WTR) astigmatism development.[1] Due to the significance of myopia, many clinical studies investigated the relationship between myopia and HOAs in cross-sectional and longitudinal study designs.[4,6-10] Previous cross-sectional studies indicated the random distribution of HOAs in myopic individuals.[6,7] However, some studies showed meaningful correlations between HOAs and myopia development.[4,8-10] Few studies investigated the relationship between astigmatism development and HOAs.[1] In a previous cross-sectional study on subjects with well-established refractive errors, it was indicated that corneal HOAs did not correlate with myopia, emmetropia, and hyperopia, but it has a meaningful correlation with astigmatism.[11] However, in that study, the relationship between the astigmatism axis and higher-order aberration was not investigated. In the current study, we aim to find correlation between HOAs, and the axis of astigmatism based on vector analysis for the astigmatism axis on subjects with well-established refractive errors.

METHODS

A cross-sectional study was conducted to investigate subjects of 18-40 years old. A total of 1370 right eyes of patients with compound myopic astigmatism who were scheduled for photorefractive keratectomy at cornea clinic in the Shiraz University of Medical Science from 2018-2020 were included. The study was approved by the Shahid Beheshti University of Medical Sciences ethics committee **(IR.SBMU.RETECH.REC.1400.1193)** and was under the tenet of the declaration of Helsinki. Informed consent was obtained from all the participants. Two drops of Cyclopentolate 1%, five minutes apart were applied for cycloplegic refraction. Cycloplegic refraction was performed 20 minutes after the second drop. Auto refraction was performed with the Nidek ARK-1 auto refractometer (Nidek Technologies, Gamagori, Japan). After performing auto refraction, the manual retinoscopy with retinoscope (Hine Beta 200, Germany) was performed. Subjective refraction after cycloplegia was taken for analysis. Comprehensive ocular examination was performed for all candidates, including dilated fundus examination, slit-lamp bio-microscopy, and applanation tonometry. Corneal imaging with the Pentacam-HR (Oculus Optik-geräte GmbH, Wetzlar, Germany) was performed for all candidates to evaluate for ectatic corneal diseases. Patients with ectatic corneal disease and any ocular conditions affecting visual acuity were not registered as candidates for refractive surgery and were excluded from this analysis.

Aberrometry for 6 mm pupil diameter was performed with a commercially available Hartmann-Shack wavefront aberrometer (Bausch & Lomb Zywave, Rochester, NY). Measurements were done after the instillation of two drops of Cyclopentolate 1%, five minutes apart to control the accommodation response. The patients were asked to perform a full blink before measurements. Total root mean square (RMS) wave-front error up to Zernike's 4th order was captured. Values for Zernike coefficients of third-order horizontal & vertical coma (Z_3^1, Z_3^{-1}), third-order oblique and vertical trefoil (Z_3^3, Z_3^{-3}), and fourth-order primary spherical aberration(Z_4^0) were available for analysis. Zernike coefficients were multiplied by -1 and transformed into the standard form recommended by the Optical Society of America.[12]

Patients older than 40 years were excluded from the study to minimize the influence of crystalline lens changes on HOAs. Additionally, individuals with simple hyperopia and compound hyperopia were excluded due to the small sample size. Given the mirror symmetry of ocular aberrations between the right and left eyes, only right-eye data were selected for analysis.

Myopia was defined as spherical refractive error <-0.50 D and astigmatism was defined as cylinder power < -0.25 D. To consider astigmatism axis, the astigmatism components were calculated as J0 and J45 with the formula of $J0 = (\text{-cylinder}/2) \times (\cos 2A)$ and $J45 = (-\text{cylinder}/2) \times (\sin 2A)$, while A= astigmatism axis. Positive values of J0 indicated WTR astigmatism and negative values of J0 indicated against-the-rule (ATR) astigmatism. To simplify evaluation, we did not consider J45 which indicates oblique astigmatism.

The required sample size for detecting a correlation was estimated using power analysis with the following parameters: power ($1 - \beta$) = 90%, significance level (α) = 0.05, and expected correlation (ρ) = 0.1. Using the formula for sample size estimation in correlation analysis (Fisher's Z-transformation) $N = [(Z_{\alpha/2}+Z_\beta)^2 \ / \ (0.5\times\ln((1+\rho)/(1-\rho)))^2] + 3$, the required sample size was 2102 participants. This ensures sufficient power to detect a correlation of 0.1 with a significance level of 0.05.

$$2102=[(1.96+1.28)^2/(0.5\times\ln((1+0.1)/(1-0.1)))^2] +3$$

Statistical analysis was performed using SPSS software version 18.2.2. (Chicago Inc., IL, USA). Descriptive statistics were applied to describe the features of the subjects studied. The Shapiro-Wilk test was used to evaluate the normality of data. Spearman's correlation test was applied to find correlations between J0 and J45 and HOAs. $P<0.005$ is considered significant.

RESULTS

The mean age was 29.01±5.19 years. The mean spherical equivalent (SEQ) was -3.64±1.59D, range [-0.75 to -10.00 D]. The mean cylindrical power was -1.01±0.95D, range [0 to -5.00D]. The demographic data of the study subjects are provided in Table 1.

The distribution of HOAs is provided in (Table 2). The total RMS value was 0.35 ± 0.17 µm, range [0.04 to 3.34 µm].The distributions of HOAs in the WTR ($J0 \geq 0$) and ATR ($J0<0$) astigmatism groups, are provided in figure 1.

A Spearman's correlation test of independence was performed to determine if J0was independent of HOAs in the studied subjects (Table 3). Significant correlations were found between J0 and vertical coma-(Z_3^{-1}) ($r = 0.1$, $P < 0.005$); J0 and oblique trefoil (Z_3^3), ($r = -0.1$, $P < 0.005$). Increasing WTR astigmatism correlated positively with vertical coma (Z_3^{-1}) and negatively with oblique trefoil (Z_3^3).

Table 1: *The demographic data of the study subjects including number of eyes, age, sphere, and cylinder.*

	Total	Simple Myopia	Compound Myopic Astigmatism	P-value
Number of eyes	1370	648	722	-
Age (year)	29.01 ± 5.19	28.85 ± 5.05	29.10 ± 5.31	0.43
Spherical Equivalent (D)	-3.64 ± 1.59	-3.31 ± 1.37	-4.07 ± 1.64	P < 0.0001
Cylinder (D)	-1.01 ± 0.95	-0.32 ± 0.18	-1.49 ± 0.84	P < 0.0001
J0	0.26 ± 0.50	.03 ± 0.14	0.50 ± 0.60	P < 0.0001
J45	0.04 ± 0.30	0.01 ± 0.11	0.07 ± 0.40	0.009

Table 2: *Distributions of higher order aberrations in the subjects studied.*

	Mean ± standard deviation	Range
Horizontal coma (Z_3^1)	0.03 ± 0.12	[-0.80 to 0.90]
Vertical coma (Z_3^{-1})	0.09 ± 0.18	[-0.70 to 0.70]
oblique trefoil (Z_3^3)	0.02 ± 0.13	[-0.70 to 0.80]
Vertical trefoil (Z_3^{-3})	-0.10 ± 0.16	[-0.80 to 0.70]
Spherical aberration (Z_4^0)	0.03 ± 0.14	[-0.80 to 0.80]
Total root means square wave-front error	0.35 ± 0.17	[0.04 to 3.34]

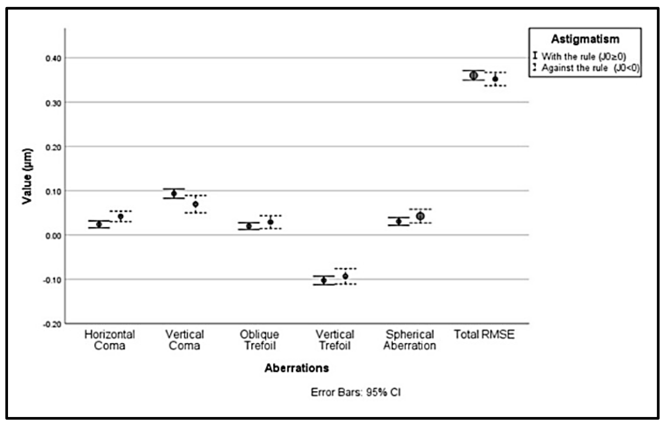

Figure 1: Distributions of higher order aberrations in with the rule and against the rule astigmatism groups based on vector analysis.

Table 3: *Spearman's correlations between refractive error components and higher-order aberrations.*

	Spherical equivalent (*r*)	J0 (*r*)	J45 (*r*)
Horizontal coma(Z_3^1)	-0.10	-0.18	-0.05
Vertical coma(Z_3^{-1})	0.02	0.10*	0.004
oblique trefoil(Z_3^3)	-0.06	-0.10*	0.10
Vertical trefoil(Z_3^{-3})	-0.007	-0.10	-0.20*
Spherical aberration(Z_4^0)	-0.02	-0.03	0.05
Total root means square wave-front error	-0.10*	0.05	0.10*

* $P <0.005$

DISCUSSION

We found weak systematic correlations between third-order aberrations and the astigmatism axis. The association between astigmatism and third-order aberrations has been reported in the previous studies.[14-17] Salman et al, found that individuals with myopic astigmatism had the highest magnitude of trefoil and coma.[16] Karimian et al, reported that vertical coma (Z3-1) and vertical trefoil (Z3-3) were the predominant aberrations in individuals with compound astigmatism.[14] Similarly, Fernández-Sánchez et al, found that large coma and trefoil values (~1µm) significantly impaired visual performance.[18]It is important to note that the magnitude of trefoil and coma aberrations in the studied subjects was small (~0.1 µm), and such small values did not interfere with visual acuity in astigmatism patients. Still, this shows the effect of astigmatism on these subjects. In the current study, we found a small but highly significant correlation between ocular third-order aberrations and the axis of astigmatism. The study showed that increasing J0 (increasing WTR astigmatism) positively correlated with vertical coma (Z_3^{-1}) and negatively correlated with oblique trefoil (Z_3^3). In line with our findings, Miller et al, found a negative correlation between J0 and oblique trefoil (Z_3^3), in a study on children with a high prevalence of astigmatism.[19] These findings suggest a systematic relationship between the axis of astigmatism and third-order aberrations. Leung et al, studied ocular aberrations and corneal shape in adults with and without astigmatism.[15] They reported that asymmetry in the corneal shape was significantly associated with the vertical trefoil (Z_3^{-3}) and vertical coma (Z_3^{-1}) of the cornea. In a multiple regression analysis, Kiuchi et al, reported that age and corneal astigmatism significantly correlated with aberrations.[11]

In a previous computational modeling study, Buehren et al, explored the interactions between higher-order aberration (HOA) patterns and sphero-cylindrical components.[1] They demonstrated that each HOA pattern induces a specific type of blur, which can be partially compensated by certain levels of spherical and cylindrical power to optimize image quality. Their findings indicated that a combination of 0.2–0.3 µm of negative vertical coma (Z3-1), positive oblique trefoil (Z3-3), and negative spherical aberration (Z4-0) results in the best retinal image quality when accompanied by myopia and with-the-rule (WTR) astigmatism.

The current study found an association between ATR astigmatism and positive oblique trefoil-(Z_3^3) and negative vertical coma-(Z_3^{-1}), which was suggested to provide a cue for WTR astigmatism development.

During the emmetropization process, high degrees of against-the-rule (ATR) astigmatism in infants and toddlers gradually decrease, with some children developing with-the-rule (WTR) astigmatism.[20] Astigmatism continues to shift throughout life, with WTR astigmatism in young adults eventually transitioning to ATR astigmatism with aging. These changes are primarily attributed to alterations in corneal curvature, though the underlying mechanisms remain unclear. The observed correlation between astigmatism axis and third-order aberrations in this study highlights the need for further investigation in infants and toddlers during the critical period of emmetropization and astigmatism development.

The study has several limitations. The exclusion of patients over 40 years limits the generalizability of findings to older populations, as crystalline lens changes could influence higher-order aberrations. The cross-sectional design prevents the assessment of longitudinal changes in astigmatism axis and higher-order aberrations over time. Other factors influencing higher-order aberrations, such as corneal biomechanics, tear film stability, and environmental influences, were not considered.

CONCLUSION

In conclusion, we found weak systematic correlations between third-order aberrations and the astigmatism axis. Increasing ATR is associated with a positive shift in oblique trefoil (Z_3^3) and a negative shift in vertical coma (Z_3^{-1}). Studying the interaction between astigmatism and HOAs in infants and toddlers who are in the age of astigmatism development is suggested.

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Patient's Consent: Researchers followed the guide lines set forth in the Declaration of Helsinki.

Conflict of Interest: Authors declared no conflict of interest.

Ethical Approval: The study was approved by the Institutional review board/Ethical review board **(**IR.SBMU.RETECH.REC.1400.1193).

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